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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/050,249	03/30/1998	HARUKI OKAMURA	OKAMURA=2B	6601

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/050,249	OKAMURA ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *93-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 30, filed on 21 March 2003 is acknowledged and entered. Following the amendment, claim 93 is amended, and claim 120 is added.

Currently claims 93-120 are pending and under consideration.

Withdrawal of Objections and Rejections:

The rejection of claim 93 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 94-119 remain rejected, and the newly submitted claim 120 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons set forth in the previous Office Actions, paper Nos. 22, 24 and 29, and for the reasons below.

Claim 94 remains indefinite for omitting essential elements. Applicants argument filed in paper No. 30 has been fully considered, but are not deemed persuasive for reasons below.

At pages 9-10 of the response, the applicant argues that the stringency of hybridization is controlled by the combination of temperature and ionic strength of the hybridization or the wash, that when only the hybridization conditions are specified, it indicates the wash conditions are less or at most equally stringent, and that accordingly, the wash temperature is not absolutely critical, and there is nothing indefinite about specifying only the hybridization conditions and not the wash conditions. This argument is not persuasive because the issue is not which, hybridization or wash, is in control, or whether a specific temperature is critical *in this particular situation*, rather, the issue is that an essential element is missing in the method steps as the art recognizes that *both* hybridization and wash conditions are in general important. Applicants may use low temperature, or low stringency in the wash step as they wish, however, they may not

omit such essential element in the claim because it would be unclear to an artisan that such omission is a result of an error or an indication of less importance.

Claim 120 is indefinite because it is unclear what is meant by "by using" in line 1. It is unclear what the IL-18 is used for, nor how it is used. The claim is further indefinite because it is unclear whether the antibody is specific for said IL-18.

The remaining claims remain rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 93, 94, 96, 118, and the dependent claims 95, 98-117 remain rejected under 35 U.S.C. 112, first paragraph, as enablement is not be commensurate in scope with the claims, for the reasons set forth in the previous Office Actions, paper No. 22, at page 4, paper No. 24, at page 3, and paper No. 29, at page 4.

Applicants argument in paper No. 30 has been fully considered, but are not deemed persuasive for reasons below.

At pages 11-12 of the response, the applicant argues that monoclonal antibodies recognizing epitopes of SEQ ID NO:2 (as in claim 93) are readily obtainable for a skilled artisan, and that it is not necessary to have either concrete information about the antibodies or the amino acid sequence of those antibodies in order to obtain them. This argument is not persuasive because neither the monoclonal antibodies recognizing epitopes of SEQ ID NO:2, nor the concrete information about obtaining the antibody is an issue of the instant rejection, rather, the issue is the antibody to "a variant thereof". Applicants further argue that structural properties would not be necessary to practice the claimed invention because they are inherent to the monoclonal antibodies, and that the use of the antibodies are disclosed in the specification. This argument is not persuasive because, once again, the main issue of the rejection is toward the antibody to "a variants thereof" (SEQ ID NO:2). As explained in the previous Office Action, the claims encompass antibodies that bind to *epitopes of the variants*, which are not found in the particularly disclosed sequence, SEQ ID NO:2, and there is no written description of those

epitopes. Therefore, the structural properties and use of the antibodies to *those epitopes* of the variants, not present in SEQ ID NO:2 are not predictable. Absent a disclosed use of those antibodies non-specific to SEQ ID NO:2, the specification fails to enable the skilled artisan to make or use the *full scope* of the subject matter of the noted claims.

Claims 93-96 and 98-118 remain rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description for the variants of SEQ ID NO:2, for the reasons set forth in the previous Office Actions, paper Nos. 22, 24 and 29.

Applicants argument in paper No. 30 has been fully considered, but are not deemed persuasive for reasons below.

At pages 13-14 of the response, the applicant argues that the present IL-18 was nominated IL-18 because it is merely the eighteenth interleukin identified, and the claimed invention is directed to a monoclonal antibody recognizing this IL-18, therefore, the present invention is a pioneer invention, and has industrial utility. This argument is not persuasive because even though the applicant is the first one to identify the eighteenth interleukin, and the similar molecule may exist in other encompassed species, as the broad genus claim is represented by *one* molecular species described with particularity in the disclosure, and no other species meeting the limitations of the claim is identified or particularly described, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, IL-18 equivalent from other species, for example. Therefore, the conception cannot be achieved. Further, there is no law or rule indicating that a pioneer discovery of a molecule in one species entitles the patent to the molecule in all mammalian species. IL-18 from different species would have distinct sequence structures, and they are patentably distinct inventions, and are not predictable from one to the other. Additionally, the industrial utility is not the issue of the rejection.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 93-119 remain rejected, and the new claim 120 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura *et al.* (*Infect. Immun.* 61: 64-70, 1993), for the reasons set forth in the previous Office Actions, paper No. 22, 24 and 29.

Applicants argument in paper No. 30 has been fully considered, but are not deemed persuasive for reasons below.

At pages 15-16 of the response, the applicant argues that the examiner is using hindsight reconstruction because one of ordinary skill in the art could not have expected to obtain a monoclonal antibody to IGIF from Nakamura's disclosure, that Nakamura is silent about whether a monoclonal antibody can be produced using the mixture, and provides no teaching about how to obtain a mAb from the mixture, and that Nakamura's antibody mixture contains other antibodies different from a mAb or the present invention. This argument is not persuasive because the issue is not how to isolate a mAb from a mixture of antibodies, and in fact, a mAb is not usually isolated from a mixture of antibodies. The state of the art at the time of the present invention was filed has well established that a monoclonal antibody to a specific protein is highly desirable because of its high specificity and easy production in large quantities, and a method of producing monoclonal antibodies had been well known and widely practiced. Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a monoclonal antibody to Nakamura's protein using the well known knowledge

and technology, and reasonably would have expected success because the method of producing monoclonal antibodies had been widely used in the art.

At pages 17-18 of the response, the applicant further argues that as evident in the specification, pages 45-46, the protein of the present claims retains activity after SDS-PAGE, and the extracting and measuring method is common knowledge in the art, and that by contrast, Nakamura's factor loses its activity after treatment on SDS-PAGE, therefore, it is a different substance. This argument is not persuasive because the specification, as written, is unclear as to whether the protein used for measuring the activity is from the gel extract. Further, *even if* that is the case, the difference in activity between Nakamura's factor and the instant protein after SDS-PAGE cannot be used as a direct evidence to conclude that the two proteins are different because other factors may contribute to this "difference", such as experimental variables as the experiments were carried out at different time, and the conditions may be different, for example, the eluting conditions and the buffer/media used, which may not favor the functional activity of the protein in Nakamura's experiment. Such experimental variables are well known in the art for causing the difference in results, and in the absence of an indication that there is no experimental variation, this single "difference" is insufficient to support that the two proteins are different. Furthermore, the evidence from the subsequent studies of Nakamura's factor by the same group provides strong support that the prior art protein is the same as that of the present invention. For example, Okamura et al. (Infection and Immunity, 1995, 63(10):3966-72) discloses a purified murine IGIF from the liver with the same physiochemical and biological properties as the claimed IGIF, and further indicates that the same molecule was also demonstrated in the serum factor that was previously reported (by Nakamura) to have an apparent molecular mass of 75 kDa by gel filtration (and 50-55 kDa on SDS-PAGE). Moreover, Okamura demonstrates that the molecular mass of 75 kDa IGIF was reduced to 19 kDa on 0.1% SDS-PAGE in the presence of DTT, and the N-terminal amino acid sequence is the same as that of IGIF from the liver, "thus IGIF in the serum sample was proved to be the same IGIF as that found in the liver exact "(the abstract, and page 3969, the second paragraph of the left column). Therefore, the protein factor of Nakamura anticipates IGIF of the present application. Additionally, a later publication from the same laboratory (Ushio *et al., J. Immunol.* 156: 4274-4279, 1996, provided by the applicants) evidences that the 18-19 kDa murine factor described in the Okamura paper has an amino acid

sequence (Fig. 2) which is identical to that shown in instant SEQ ID NO: 2. In view of the similar sources and the identity of structural, biophysical, and functional properties of the instantly claimed protein and the 18-19 kDa factor described in the Okamura and Ushio papers, it reasonably appears that they are the same. With respect of the argument that the extracting and measuring method is common knowledge in the art, it is not the issue of the rejection.

Conclusion:

No claim is allowable.

Advisory Information:

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
5/15/03